

REMARKS

Claims 30-59 are pending. The Office finds that claims 30-33 are allowable and that claims 47-99 would be allowable if rewritten in independent form. Office Action, page 8. Applicants acknowledge with appreciation the Office's withdrawal of the previous rejections under 35 U.S.C. §§ 102 and 103. Applicants address each new rejection below, according to its statutory origin.

Anticipation Rejection

Claims 34, 35, 38-40, 42-46, and 50-59 stand rejected under 35 U.S.C. § 102(e) in light of U.S. Patent 5,763,158 ("Bohannon"). Office Action, page 3. According to the Office, Bohannon teaches a method of detecting an analyte in a sample comprising the steps recited in independent claim 34. When referring to the "sample" recited in claim 34, the Office cites to the "ligand" discussed in Bohannon. *Id.* The Office contends that Bohannon teaches a first reagent comprising an ECL label at col. 4, lines 10-60. *Id.* The second reagent having an ECL quenching moiety as described in claim 34 is allegedly taught at col. 4, lines 35-46. The Office specifically points to the apparent teaching of rhodamine as a quencher and notes that rhodamine contains a benzene moiety. *Id.* When discussing steps b-d of claim 34, the Office cites to col. 4, lines 15-21 for contacting an electrode and applying a potential to the electrode and to lines 30-35 for detecting a difference in ECL emissions. *Id.* at page 4. Applicants traverse this rejection, as the Office's interpretation of Bohannon is flawed for several reasons.

Contrary to the Office's interpretation of Bohannon, this reference does not teach rhodamine as an ECL quencher. Bohannon does not provide any structural identification of an ECL quencher. When discussing rhodamine as a quencher,

Bohannon discusses it as part of “other” reporter-quencher systems aside from the ECL system described in the prior paragraph. Col. 4, lines 36-38. Clearly, Bohannon did not contemplate using rhodamine as an ECL quencher. Specifically, the reference suggests that rhodamine can be used as a quencher with fluorescein dye, which is a fluorescent label, not an ECL label. Col. 4, lines 41-42.

When addressing ECL quenchers, Bohannon only discusses such quenchers in functional terms, as a substance that absorbs light at 620 nm or destabilizes the ECL compound when in close proximity. Bohannon also appears to suggest that a quencher may operate by destabilizing a ruthenium compound. Col. 4, lines 24-28. Applicants note that the Office’s description of Bohannon’s alleged teaching with regard to quenchers is also in functional terms. Office Action, page 6, lines 2-4. This is likely because at the time the application that lead to the Bohannon patent was filed, ECL technology was a “recently developed” technology. Col. 4, lines 8-11. Applicants also note that the specification explains that few ECL quenchers were known at the time of the instant invention. See specification at paragraph 58. In light of this background, there is no reason to believe that Bohannon thought of rhodamine as an ECL quencher. Indeed, rhodamine dyes do not absorb at 620 nm. Absorption of light at 620 nm is a feature of ECL quenchers, according to Bohannon. Col. 4, lines 24-28. Applicants attach absorption spectra for the three rhodamine dyes, rhodamine 123, rhodamine 6G, and rhodamine B as provided by the Oregon Medical Laser Center’s web site: <http://omlc.ogi.edu/spectra/PhotochemCAD/html/index.html>. Moreover, neither benzene, benzoquinone, nor phenol absorb at 620 nm, as shown in the attached graph. Thus, like the rhodamine dyes, Bohannon would not consider the quenchers contemplated in the pending claims to be ECL quenchers. The fact that Bohannon did

not list rhodamine as an ECL quencher supports Applicants' assertion that it was not recognized as an ECL quencher. In sum, because Bohannon does not expressly or implicitly describe an "ECL quenching moiety comprising at least one benzene moiety" as required by claim 34, this reference cannot anticipate claim 34 or its rejected dependent claims 35, 38-40, 42-46, and 50-59.

In addition, Bohannon does not teach a labeled analyte. Rejected claims 43, 44 and 50-57 describe an ECL labeled analyte. In its interpretation of Bohannon, the Office has misinterpreted the meaning of the term "ligand" as used in this reference. Specifically, the Office incorrectly considers Bohannon's ligand as analogous to the analyte recited in claim 34. Instead, Bohannon's "target molecules" appear to be more closely related to the specification's use of the term "analyte." At paragraph 129, the specification defines an analyte as "a substance which is to be detected and preferably quantified." Bohannon explains that "antigens or antibodies detectable by the invention are referred to as target molecules. . . ." Col. 3, lines 19-21. In contrast, Bohannon defines ligands as "a small molecule capable of binding to a target antigen or antibody molecule or a small molecule that is a specific binding partner of an antibody specific for a target antigen or antibody." Col. 3, lines 36-39. Indeed, Figures 1 and 2 of Bohannon clearly show that the ligand is tethered to a solid support and thus cannot be an analyte present in a sample. See col. 5, lines 6-23 where item 121 is a ligand that is part of a ligand-enzyme complex (item 12) that is attached to a solid support (item 14) via a linker (item 141). Thus, a ligand in Bohannon is not an analyte, but a reagent that can bind to an analyte.

Indeed, in every instance where Bohannon discusses the use of a label, whether it be an enzyme or a reporter molecule, that label is attached to a ligand. Nowhere in

Bohannon does the reference teach or suggest that a label should be attached to an analyte, as recited in dependent claims 43, 44, and 50-57. Thus, for these reasons, Bohannon cannot anticipate claims 43, 44, and 50-57. Applicants request that the Office withdraw this rejection.

Obviousness Rejection

The Office rejects claims 36, 37, and 41 as obvious in light of Bohannon and Kuzmin et al., *J. Photochem. Photobiol. A: Chem* 87:43-54 (1995). Office Action, page 5. The Office uses Bohannon as described above, acknowledging that this reference does not teach quinones or phenols as quenchers or an ECL label comprising osmium. Office Action at page 6. The Office turns to Kuzmin for allegedly teaching quinones as quenchers and asserts that quinones encompass phenols. *Id.* at page 7. The Office also notes that Kuzmin does not provide any examples of assays using an osmium label, but contends that Kuzmin teaches ruthenium and osmium as equivalents. *Id.* In light of these alleged teachings, the Office concludes that it would be obvious to substitute quinone and phenolic quenchers into Bohannon's assay and to use osmium as an ECL label in Bohannon's assay. Applicants note that the Office has not provided any rationale as to why the skilled artisan would be motivated to combine these references and be successful in arriving at the claimed invention.

As discussed above and noted by the Office, Bohannon describes ECL quenchers functionally as a substance that absorbs light at 620 nm. Office Action at page 6. In contrast, even if Kuzmin did show that quinone functioned as an ECL quencher, the skilled artisan would not be led to a particular compound such as quinone based on the general functional description given in Bohannon. Moreover,

Kuzmin studies fluorescence, not electrochemiluminescence, and uses a method that does not involve an electrode to make measurements. Instead, Kuzmin uses a spectrophotometer or a spectrofluorometer to measure fluorescence lifetimes. See page 44, right column. Applicants note that the Office appears to agree with this interpretation of Kuzmin, as the prior anticipation and obviousness rejections based on this reference were withdrawn. See Office Action at page 9. Thus, there is no connection between the suggested use of ECL labels in Bohannon and the fluorescence studies in Kuzmin. Because the two references discuss two different phenomena (ECL v. fluorescence), the skilled artisan would not be motivated to use an alleged fluorescence quencher as an ECL quencher.

Finally, as Applicants have previously explained, the Office's cite to Kuzmin at page 51, right column, paragraph 4 does not suggest that osmium and ruthenium are equivalents. This section of Kuzmin discusses an apparent inconsistency in the data. Based on ΔG values, it appeared that the sample reactants were in a polar microenvironment. But the spectral properties of RuL_6^{2+} suggested a low polarity environment. Kuzmin provides an explanation for this discrepancy, discussing the localized effect water molecules might have on RuL_6^{2+} . In this discussion, Kuzmin notes a study looking at the isotope effect on the lifetimes of osmium (Os) and ruthenium (Ru) complexes and micellar solutions showed that about 30% of the ligand surface of RuL_6^{2+} was accessible to water molecules. Assuming that Kuzmin's description of this study is accurate, this study addresses the behavior of Os and Ru compounds in micellar environments. This study does not, however, address the ability of Os compounds to act as ECL labels as recited in claim 41 let alone show an equivalence between the two metals in the context of an ECL label. Thus, the motivation to use Os

instead of Ru in Bohannon's assay does not exist. Because the combination of Bohannon and Kuzmin does not render the rejected claims obvious, Applicants request that the Office withdraw this rejection.

Statement on Allowability

At page 8 of the Office Action, the Office dismisses Bohannon as applied to allowed claims 30-33 because Bohannon allegedly does not teach detection of nucleic acids.¹ Based upon Applicants' reading of Bohannon, this reference does appear to contemplate a nucleic acid target molecule (i.e., an analyte) or a reagent that binds to a target molecule (i.e., a ligand). See col. 3, lines 26-27 and 43-45. Bohannon, however, still fails to anticipate claims 30-33 because this reference does not teach phenol or benzoquinone as an ECL quencher as recited in claims 30-33. Bohannon's limited and generalized teaching on ECL quenchers would not point the skilled artisan towards particular quenchers such as phenol and benzoquinone.

Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of pending claims 30-59.

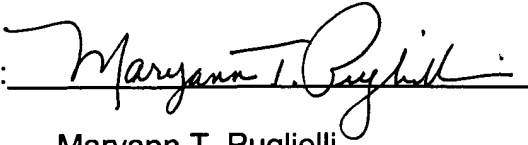
¹ Applicants note that the Office also discusses claims 43-59 as allowable subject matter. Applicants believe that the Office's inclusion of claims 43-59 as allowable subject matter may be unintentional, as claims 43-46 and 50-59 stand rejected. Applicants request clarification on this point.

Please also grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

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By: 
Maryann T. Puglielli
Reg. No. 52,138